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Editorial

Biomarkers of Esophageal Cancer Comes of Age?

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EDITORIAL

Despite improvements in surgical techniques, adjuvant chemotherapy and radiotherapy, many patients with esophageal carcinoma still suffer rapid recurrence of the disease and a poor prognosis [1]. Biomarkers should be useful tools to evaluate biological features of esophageal carcinoma to predict recurrence and/or patients' survival [2]. Basically, thoracic esophageal squamous cell carcinoma (SCC) has very similar biological character to head & neck SCC. Moreover, thoracic esophageal adenocarcinoma has very similar to esophago-gastric junction adenocarcinoma. Based on development of various companion biomarkers for molecular targeting agents for head & neck SCC and/or gastric adenocarcinoma, potential biomarkers, recently, have been reported for esophageal cancer [3-6].

DNA hypermethylation of the tumor suppressor gene, histone modifications, histonemethylationand clinicopathological significance of microRNAs in esophageal SCC have been reported [3]. Numerous molecular changes occur during the multistage conversion of Barrett's metaplasia to dysplasia and adenocarcinoma. Epigenetic changes, especially changes in DNA methylation are widespread during this process. Aberrant DNA methylation has been shown to occur at promoter's oftumor suppressorgenes,adhesionmoleculesandDNArepairgenesduring Barrett's esophagus. These epigenetic alterations can be used as molecular biomarkers for risk stratification and early detection ofesophagealadenocarcinoma. Inactivation of cell-cycle regulating tumor suppressor gene p16, resulting from epigenetic alteration, is one of the most common in the carcinogenesis of esophageal carcinomas. DNAmethylationof p16 gene, which indicated potential application of this biomarker in early detection as well as the prognosis of esophageal carcinoma, frequently elevated in esophageal carcinoma [7]. The data so far on miRNAs inesophagealcarcinogenesis is also promising for diagnosis and treatment [8]. DifferentialmiRNAprofiles and aberrant protein glycosylation in tissue samples have been reported to improve performance of existing tissue-based diagnostic biomarkers [9].

Malignant potential of esophageal carcinoma has been attributed frequently to high levels of angiogenic factor and/or growth factor expression, such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), hepatocyte growth factor (HGF), thymidine phosphorylase (TYMP), and midkine [10]. High inflammatory mediators also contribute malignant potentials [5,6]. These biomarkers, as well as receptors for these molecules, were useful not only for treatment but also for diagnosis. These diagnostic molecular markers for esophageal carcinoma were classified into two categories; carcinogenesis & risk biomarkers [5,6], and treatment response biomarkers [11]. Anti-angiogenic factors and anti-growth factor receptors are both promising approaches to deal with advanced esophageal carcinoma. Since esophageal carcinoma frequently over-express TYMP, TYMP targeting 5-FU derivatives, capecitabine, may be a good chemotherapeutic option [12] same as gastric cancer. These angiogenic factors were biomarkers to predict poor treatment response to radiation and/or chemotherapy [11].

Based on the development of immunotherapy for gastrointestinal carcinomas, several tumor-testis antigens have been reported to be target biomarkers for esophageal cancer [13,14]. Measurement of an autoantibody response to tumor-associated antigens, to help discriminate early-stage esophageal SCC patients from normal controls, may aid in early detection of esophageal SCC [2,14]. Since serum autoantibodies precisely react to micro-residual cancer cells, these markers may be a good tool to predict recurrence and patients' survival. Initial trials validating new immunotherapeutic approaches, including vaccination-based and adoptive cell therapy strategies, for gastrointestinal malignancies have demonstrated safety and the induction of antitumor immune responses. Therefore, immunotherapy is at the forefront of neoadjuvant as well as adjuvant therapies for the treatment and eradication of esophageal carcinoma. Recently, the safety and immunogenicity of NY-ESO-1 vaccine were confirmed on the patients with NY-ESO-1 expressed tumors [15].

Under current conditions, biomarkers of esophageal carcinoma have been developed to improve quality of early diagnosis, monitoring of disease, and predicting patients' survival. Moreover, several biomarkers have become to be molecular targets of treatment.

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